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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/492,954	01/27/00	PYLE A	58077/JPW/JS

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EXAMINER	
WILDER, C	

ART UNIT	PAPER NUMBER
1655	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/492,954	Applicant(s) Pyle et al.
	Examiner CB Wilder	Group Art Unit 1655

☒ Responsive to communication(s) filed on *Jan 27, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-8* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-8* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Drawings

1. The drawings are objected to because the description in the specification under "Brief Description of the Figures" for each of the figures do not coincide with the drawings. The informalities include the following:

(a) In Figure 3, a label distinguishing Figure 3A is missing.

(b) In Figure 4, a label distinguishing Figure 4A and 4B is missing.

(c) In Figure 6, a label distinguishing Figure 6A, 6B and 6C is missing.

(d) Figure 9 is unlabeled.

Correction is required.

Objection

2. The specification is objected to because of the following informalities:

(a) The word "Breif" in the "Brief Description of the Figures" at page 5, line 1 is misspelled. It is suggested changing "Breif" to "Brief".

(b) The word "neucleoside" is misspelled at page 3, line 12.

Appropriate correction is required.

3. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the

remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 4-6 at page 44 of the specification have been renumbered to claims 1-3.

Claim Rejections - 35 USC § 112

4. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-6 are indefinite for "being capable of" in claim 1, step (a) because it cannot be determine whether "capable of" is a property of the first label or a method step. It is suggested deleting "being capable of".

(b) Claims 1-6 are confusing in claim 1 at step (b) because step (b) appears to be redundant to step (a) and it cannot de determined how the method steps differ. Clarification is required.

(c) Claims 1-3 are confusing at "first label" because it appears that multiple labels are used in the method, but only one label is disclosed. It is suggested inserting after "a second RNA" in claim 1, step (a), "having a second label attached thereto" as suggested in the specification at page 14.

(d) Claims 1-6 are rejected as being incomplete for omitting an essential element in claim 1, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted element is a step in claim 1 wherein ATP and a divalent cation are required for RNA helicase to unwind the

RNA duplex as recited in the specification at page 38, subheading "Helicase Reaction". Additionally, Shuman also teaches that ATP and a divalent cation are required for helicase activity (10936, lines 40-52). Therefore, it is suggested combining claims 1 and 2.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuman (Proc. Natl. Acad. Sci. USA, November 1992), in view of Bjornson et al. (Biochemistry, December 1994). Regarding claim 1, Shuman discloses a method for detecting the release of a single-stranded RNA from an RNA duplex which comprise (a) admixing an RNA helicase with the RNA duplex under conditions permitting the RNA duplex to unwind the RNA duplex and release single stranded RNA, wherein the RNA duplex comprises a first RNA having a label and a second RNA wherein the unwound single-stranded RNA released from the duplex is detected by gel electrophoresis (page 10936 col. 1, lines 18-29 and 40-52, see Figure 1 and Figure 2). The method of Shuman differs from that of the claimed invention in that Shuman does not teach wherein the first label is capable of producing a luminescent energy pattern when the first RNA is present in the RNA duplex which differs from the luminescent pattern produced when the first RNA is not present in the RNA duplex.

The reference also does not teach detecting a change in the luminescent energy pattern produced by the first label to thereby detect release of a single-stranded RNA from the RNA duplex. Bjornson et al. (Biochemistry, December 1994) teach a method for detecting the release of a single stranded DNA molecule from a DNA duplex comprising admixing a helicase with a DNA duplex under conditions permitting the helicase to unwind the duplex and release single stranded DNA, wherein the first strand of the DNA substrate I has a label attached thereto at the 3' end and the second strand of the DNA substrate I has a label attached thereto at its 5' end, wherein the first label is capable of producing a luminescent energy pattern, detecting changes in the luminescent energy pattern produced by the first label so as to thereby detecting release of single-stranded DNA from the DNA duplex (page 14309, last paragraph col. 1 to first paragraph col. 2, see also page 14310, Figure 2). It would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Shuman with the teaching of Bjornson et al. to obtain the claimed invention because the skilled artisan would have been motivated to improve the method of Shuman by incorporating a label useful in a fluorescence based assay to detect the release of single stranded RNA from the RNA duplex with a reasonable expectation of success by the teaching of Bjornson et al. that a fluorescent based assay has several obvious advantages for kinetic studies in general and particularly for mechanistic studies for helicase-catalyzed unwinding. First, such an assay is extremely sensitive (Abstract), allowing unwinding to be monitored continuously in real time. Second, a full kinetic time course can be obtained from a single experiment with more accurate determination of the observed kinetic parameters, third the data can be easily imported into numerical simulation programs

and fourth, one can perform an experiment over a much wider range of substrate concentrations (page 14312, col. 1, lines 112-44). Although Bjornson et al. do not mention the fluorescent assay being used for detecting single stranded RNA from RNA duplexes, Bjornson et al. do mention that the advantages of a fluorescent based study will greatly facilitate the detailed kinetic studies that are need to understand the mechanism(s) by which helicases (implying both RNA and DNA helicases) carry out their essential function (page 14313, col.2, first paragraph). Additionally one of skill in the art would be motivated to incorporate a label capable of producing a luminescent energy pattern for the obvious benefits which incudes cost-effectiveness, commercial availability and non-toxicity.

Regarding claim 2, Shuman discloses wherein the conditions which permit the RNA helicase to unwind the RNA duplex and release the single stranded RNA comprise the presence of ATP and a divalent cation, e.g., Mg^{2+}, Co^{2+}, and Mn^{2+} (page 10936, col. 1, lines 40-52).

Regarding claim 3 and 4, Bjornson et al. teach wherein a label is present at the 3' end of the first stand of the DNA and a different label is attached to the second strand of the DNA at the 5'end and the luminescent energy pattern results from the interaction of luminescent energy released from the two different labels (page 14309 col. 2, lines 1-28 see also Figure 1).

Regarding claim 5, Bjornson teach wherein the two labels comprise fluorophors and the second label absorbs luminescent energy released from the first fluorophor (page 14309, Figure 1).

Regarding claim 6, Bjornson et al. teach wherein the first label is fluorescein (donor) and the second label is hexachlorofluorescein (acceptor) (page 14309, Figure 1 and 14310, Figure 2). The

choice of a first and second label would have been determined by the skilled artisan based on commercial availability, experimental procedures and desired results.

Regarding claim 7, Bjornson et al. disclose a method of measuring the rate of release of DNA from a DNA duplex which comprise detecting whether single stranded DNA is released from the duplex at predetermined time intervals and determining the rate of release of the single stranded DNA from the duplex (page 14310, Figure 2 and col. 2, first and second full paragraphs).

Regarding claim 8, Shuman discloses a method of determining whether a compound is capable of modulating the release of a single stranded RNA from an RNA duplex by an RNA helicase which comprise detecting the release of the single stranded RNA from the RNA duplex, wherein the compound (AMPPNP or AMPPCP) is added to the mixture comprising the RNA helicase, RNA duplex and label (page 10937, figure 5)

Prior Art

7. The prior art made of record is considered pertinent to applicant's disclosure. Kowalczykowski et al. (5,747,247 May 5, 1998) disclose a method for detecting helicase activity and inhibition using luminescent markers (labels).

Conclusion

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the Exr. should be directed to Exr. Cynthia Wilder whose telephone number is (703) 305-1680. The Exr. can normally be reached on Monday through Thursday from 7:00 am to 5:00 pm.

If attempts to reach the Exr. by telephone are unsuccessful, the Exr.'s supervisor, W. Gary Jones, can be reached at (703) 308-1152. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed the Group's receptionist whose telephone number is (703) 308-0196.

Cynthia Wilder

Cynthia B. Wilder, Ph.D.

June 26, 2000

S. Gitomer

PRIMARY EXAMINER